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(liposome adj5 complex) same (dna or gene) same (drug)	59

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L2 (liposome adj5 complex) same (dna or gene) same (drug)

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1381

L1

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L2: Entry 43 of 59

File: USPT

Dec 28, 1999

DOCUMENT-IDENTIFIER: US 6008202 A

**** See image for [Certificate of Correction](#) ****

TITLE: Stable lipid-comprising drug delivery complexes and methods for their production

Detailed Description Text (42):

Assays utilized in determining the biological activity of the complexes vary depending on what drug is contained in the complexes. For example, if the drug is nucleic acid encoding a gene product, the biological activity can be determined by treating cells in vitro under transfection conditions utilized by those of ordinary skill in the art for the transfection of cells with admixtures of DNA and cationic liposomes. Cells which may be transfected by the complexes includes those cells which may be transfected by admixture DNA/liposome complexes. The activity of the stored complexes is then compared to the transfection activity of complexes prepared by admixture. If the drug is a protein, then activity may be determined by a bioassay suitable for that protein.

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L2: Entry 39 of 59

File: USPT

Jan 9, 2001

DOCUMENT-IDENTIFIER: US 6171614 B1

**** See image for [Certificate of Correction](#) ****

TITLE: Synthesis of glycopospholipid and peptide-phospholipid conjugates and uses thereof

Detailed Description Text (57):

Liposomes prepared with glycopospholipid or peptide-phospholipid conjugates of the invention are also useful in gene therapy to transfer DNA through a membrane to a desired cellular location. The efficiency of the use of liposomes as delivery agents for DNA and other nucleosides, nucleotides, polynucleotides, etc. depends on such factors as tissue type, lipid membrane composition, ratio of lipid to DNA, stability of the DNA-lipid complex, etc. Recently, cationic lipids have been used as DNA delivery agents. Because the negative charges of a DNA backbone can interact with the positive charges of cationic lipids, DNA-liposome complexes are formed wherein the DNA can interact stably with the lipid on either the inside or outside of the liposome. The DNA may also become enclosed by the lipid and lie freely in the aqueous internal compartment, similar to encapsulation of toxic drugs. Because the positioning of DNA relative to the liposome depends on the composition and structure of the DNA-lipid complexes, the most effective method of DNA-lipid complex formation may be to design a specific complex for a 1:5 designated role, such as tissue targeting.

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Terms	Documents
L12 and cosmetic\$	20

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L14

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<u>L14</u>	L12 and cosmetic\$	20	<u>L14</u>
<u>L13</u>	L9 and \$carnitine	21	<u>L13</u>
<u>L12</u>	L11 and 424/450.ccls.	207	<u>L12</u>
<u>L11</u>	liposome same (gene or dna) same drug	1330	<u>L11</u>
<u>L10</u>	L9 and 424/450.ccls.	255	<u>L10</u>
<u>L9</u>	liposome same (gene or nucleic or dna) same drug	1578	<u>L9</u>
<u>L8</u>	L7 and cosmetic\$	2	<u>L8</u>
<u>L7</u>	\$carnitine same liposome same drug	12	<u>L7</u>
<u>L6</u>	L4 and drug	97	<u>L6</u>
<u>L5</u>	L4 and cosmetic\$	83	<u>L5</u>
<u>L4</u>	\$carnitine same liposome	101	<u>L4</u>
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<u>L2</u>	carnitine same liposome	19	<u>L2</u>
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L12: Entry 68 of 207

File: USPT

Mar 12, 2002

DOCUMENT-IDENTIFIER: US 6355267 B1

**** See image for [Certificate of Correction](#) ****

TITLE: Liposome preparation and material encapsulation method

Brief Summary Text (3):

The present invention relates generally to liposomes, and more particularly to a method of producing liposomes useful for encapsulating biologically active materials. The liposomes are, therefore, useful in applications such as in vivo drug delivery and gene therapy and as diagnostic agents.

Current US Original Classification (1):424/450

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L14: Entry 17 of 20

File: USPT

Aug 5, 1997

DOCUMENT-IDENTIFIER: US 5653996 A

TITLE: Method for preparing liposomes

Detailed Description Text (2):

This invention describes new and useful methods for the preparation of liposomes for use in the delivery of therapeutic, diagnostic or cosmetic agents. The present invention provides an economic and efficient method of preparing liposomes on a large scale.

Detailed Description Text (18):

The term "biologically active molecule" is defined herein as a naturally occurring or synthetic compound which has an effect on an organism to which it is administered. Representative examples of biologically useful polypeptides include, among others, nucleoproteins, glycoproteins, and lipoproteins. Liposomes made according to this invention are also used to delivery nucleic acids for gene therapy, to provide properly functioning replacement genes, or to introduce a new or enhanced gene functionality. Many protein classes are suitable for use in this process, including antibodies, enzymes, hormonally active polypeptides, immune modulators such as lymphokines, monokines and cytokines, growth regulatory and stimulatory proteins, blood proteins, and antigens for viral, bacterial and parasitic vaccines. Specific examples of suitable proteins include alpha-, beta- and gamma-interferon, tumor necrosis factor-alpha and tumor necrosis factor-beta, plasminogen activators such as tissue plasminogen activator or urokinase or streptokinase, relaxin, immunoglobulins, CD4, TGF-.alpha. and TGF-.beta., DNase, VEGF, NGF, NF, activin, inhibin, EGF, IGF, enkephalinase, blood clotting factors including factor VIII and tissue factor as well as fragments or amino acid sequence variants thereof and antibodies thereto. Examples of other biologically active molecules that can be used in this process include steroids, lipids, synthetic and naturally occurring drugs, tumoricidal agents (such as doxorubicin) nucleic acids, and amino acids.

Detailed Description Text (20):

Cosmetics or cosmetic ingredients such as hair sprays, colorants, dyes, and the like are appropriate for incorporation into a liposome. Medicaments used in mouthwashes, throat sprays, antiseptic sprays and the like are also suitable for use in the practice of this invention.

Detailed Description Text (44):

D. Liposome Sizing. Without being limited to a particular theory of operation, it is believed that the clearance rate of liposomes from blood or tissue depends on their particle size as well as the specific ingredients they contain. In certain embodiments, liposomes are selected for therapeutic administration which are approximately 50-100 nm in diameter, or larger. In other embodiments, faster clearance is desired or smaller size is advantageous for other reasons, and liposomes are selected of less than 50-nm diameter. The size of the liposome may also be related to its stability; in some embodiments for example, a larger size liposome can be relatively unstable, compared to a smaller liposome, and the selection criteria may take advantage of this feature. For example, a relatively large sized and relatively unstable liposome may be useful for administration of pharmaceuticals in the lung, where instability leads to rapid spreading of

components. The size of the liposome for any particular application, whether therapeutic, diagnostic, commercial, industrial, or cosmetic, shall be selected according to the characteristics desired.

Detailed Description Text (55):

This invention provides novel methods for the preparation of liposomes which can be used in a variety of formulations and for a variety of diagnostic, commercial, cosmetic, industrial, and therapeutic uses.

Detailed Description Text (68):

Liposome foams can be prepared using conventional two-chamber propellant devices, such as are used for cosmetic foams, such as shaving cream or hair-styling mousse. A heavy liposome suspension contained in one chamber is mixed with propellant gas contained in a second chamber, and the gassified mixture or foam is expelled under the propellant release pressure through a discharge nozzle. U.S. Pat. No. 3,326,416 describes a two-chamber propellant foam device which could be readily adapted for use in liposome foam generation.

Current US Original Classification (1):

424/450

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L14: Entry 15 of 20

File: USPT

May 19, 1998

DOCUMENT-IDENTIFIER: US 5753263 A

TITLE: Method to deliver compositions conferring resistance to alopecia to hair follicles

Abstract Text (1):

The invention describes a method to deliver a composition selectively to hair follicles using a liposomal formulation. Proteins which are cell cycle inhibitors are products of the multi-drug resistance gene or the recombinant materials for their production are targeted to hair follicles by encapsulating them in liposomes.

Brief Summary Text (36):

The invention further describes a method of directly and selectively delivering a beneficial compound to hair follicles of a mammal comprising the step of applying a liposome composition of this invention topically to skin areas of a mammal having a plurality of hair follicles, wherein the liposome composition comprises a liposome containing an effective amount of at least one selected beneficial compound and wherein the beneficial compound is a macromolecule, a lipophobic molecule or a lipophilic molecule having undesirable effects on cells external to said hair follicles. The liposome composition may be applied to the skin area of a mammal having a plurality of hair follicles either in vivo, or in vitro, using explanted skin tissue. The explanted skin tissue may be grown, for example, as described herein, in skin histoculture. In preferred embodiments, the beneficial compound is a hair color-restoring agent such as melanin, hair dye, or tyrosinase. In related embodiments, the beneficial compound is a hair growth stimulator such as cyclosporin-A, or related compounds, finasteride, or an antisense nucleic acid molecule that would block a gene conferring a negative effect to the hair. Techniques of designing antisense molecules are well known to those of ordinary skill in the art. Hair growth stimulating compounds may have undesirable side effects when delivered systemically, one advantage of the present invention provides compounds for and a method of directly and selectively delivering the compounds to the hair follicle cells without substantially delivering the compound to the bloodstream, thus avoiding such undesirable side effects. In another related embodiment, the beneficial compound is a nucleic acid capable of expressing an effective amount of a replacement therapy protein. Particularly preferred are nucleic acid molecules capable of expressing tyrosinase or hair-growth stimulating proteins or the multi-drug resistance proteins conferring resistance to chemotherapy-induced alopecia.

Detailed Description Text (100):

A preferred embodiment involves the prevention of hair loss (alopecia) during chemotherapy where a patient experiences chemotherapy-induced hair loss due to the effect of the chemotherapeutic agent on the hair follicle and surrounding tissue. Thus the invention contemplates the use of inhibitors of the deleterious effects of a chemotherapeutic agent. By virtue of the selective application of the inhibitor to the hair follicle by the liposome-mediated delivery methods of the present invention, inhibition of a chemotherapeutic agent is localized to the hair follicle and therefore does not interfere with the intended systemic activity of the administered chemotherapeutic agent. In this embodiment, a preferred inhibitor of chemotherapy-induced alopecia is a gene product of the multiple drug resistance

(MDR) gene, preferably the p-glycoprotein expressed by the human MDR-1 gene. Administration of a nucleic acid comprising an expression vector capable of expressing human p-glycoprotein via liposomes to the hair follicle provides intracellular human p-glycoprotein, and reduces the toxic effects of the chemotherapy upon the hair follicle, thereby reducing alopecia induced by the chemotherapy.

Detailed Description Text (269):

FIG. 14 shows that after topical application of liposome-Lac-Z, the expression of the Lac-Z gene, indicated by blue staining of the X-gal substrate, was in the hair-forming hair matrix cells in the hair follicle bulbs (FIG. 14 a-c) and in the bulge area (FIGS. 14d & e) below the opening of the sebaceous gland, which is thought to contain the follicle stem cells (Cotsralelis et al., Cell 61:1329-1337, 1990). The transfection frequency was high since many follicles are stained by X-gal (FIG. 14a). No other cells were transfected with Lac-Z outside the follicle in the dermis or epidermis (FIG. 14a). FIG. 14b demonstrates the expression of the Lac-Z gene in the hair matrix cells. The extensive Lac-Z expression in the hair matrix cells can be seen very clearly at high magnification (FIG. 14c). The transfection of what may be follicle stem cells can be seen in FIGS. 14 d & e. The introduction of active genes in stem cells is important for long-term modification of the hair follicle. Topical application of the naked Lac-Z gene did not result in gene transfer and no Lac-Z staining can be seen in follicles in animals not treated with liposome-Lac-Z (data not shown). These results demonstrate that genes can be selectively targeted to the most important cells of the hair follicle by liposomes. The targeting of the reporter gene to the hair follicle cells is the most selective targeting of a gene observed thus far in vivo (Caplen et al., Nature Med. 1:39-46, 1995). The high hair-follicle selectivity of gene targeting by topical liposome application suggests the feasibility of gene targeting of hair matrix cells and possibly follicle stem cells to restore hair color such as with the tyrosinase gene (Shibahara et al., J. Exp. Med. 156:403-405, 1988; Tanaka et al., Development 108:223-227, 1990) and with genes to restore hair growth. The high selectivity of topical liposome gene targeting is also important for safety and cosmetic reasons.

Current US Original Classification (1):

424/450

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L3: Entry 4 of 6

File: EPAB

Feb 4, 1994

DOCUMENT-IDENTIFIER: FR 2694195 A1

TITLE: Compsns. for removing subcutaneous fat - contg. coenzyme A, carnitine and caffeine

Abstract Text (1):

CHG DATE=19990617 STATUS=O>Cosmetic compsns. for slimming treatment contain a mixt. of coenzyme A (I), carnitine and caffeine. The mixt. pref. contains 0.001-5% (esp. 0.01-1%) of (I), 0.1-95% (esp. 0.1-20%) of carnitine, 0.1-10% (esp. 0.1-2%) of caffeine, and 0.05-5% palmitoylcarnitine (II). (I) is produced by chemical synthesis, tissue extraction or microbial fermentation and is used in pure form or as a soln.. The compsns. contain 0.1-30% (esp. 1-10%) of the mixt. and are formulated as powders, solns., dispersions, emulsions, capsules, particles, microsponges, liposomes, gels, milks, creams, lotions or masks. USE/ADVANTAGE - The compsns. may be used to remove subcutaneous fat. (I) potentiates the lipolysis-promoting effects of carnitine and caffeine.

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L5: Entry 81 of 83

File: EPAB

Feb 4, 1994

PUB-NO: FR002694195A1

DOCUMENT-IDENTIFIER: FR 2694195 A1

TITLE: Compsns. for removing subcutaneous fat - contg. coenzyme A, carnitine and caffeine

PUBN-DATE: February 4, 1994

INVENTOR-INFORMATION:

NAME

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DANIEL, GREFF

ASSIGNEE-INFORMATION:

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SEDERMA SA

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APPL-NO: FR09209598

APPL-DATE: July 30, 1992

PRIORITY-DATA: FR09209598A (July 30, 1992)

INT-CL (IPC): A61K 37/48

EUR-CL (EPC): A61K008/44; A61K008/49, A61K008/60 , A61Q019/06

ABSTRACT:

CHG DATE=19990617 STATUS=O>Cosmetic compsns. for slimming treatment contain a mixt. of coenzyme A (I), carnitine and caffeine. The mixt. pref. contains 0.001-5% (esp. 0.01-1%) of (I), 0.1-95% (esp. 0.1-20%) of carnitine, 0.1-10% (esp. 0.1-2%) of caffeine, and 0.05-5% palmitoylcarnitine (II). (I) is produced by chemical synthesis, tissue extraction or microbial fermentation and is used in pure form or as a soln.. The compsns. contain 0.1-30% (esp. 1-10%) of the mixt. and are formulated as powders, solns., dispersions, emulsions, capsules, particles, microsponges, liposomes, gels, milks, creams, lotions or masks. USE/ADVANTAGE - The compsns. may be used to remove subcutaneous fat. (I) potentiates the lipolysis-promoting effects of carnitine and caffeine.

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